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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/551,466	08/07/2006	Ji Hoon Jeong	2236.0180000/JUK/SMW	4435

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EXAMINER	
PITRAK, JENNIFER S	

ART UNIT	PAPER NUMBER
1635	

MAIL DATE	DELIVERY MODE
11/09/2009	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/551,466	JEONG ET AL.	
	Examiner	Art Unit	
	JENNIFER PITRAK	1635	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *26 August 2009*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-4 and 6-14* is/are pending in the application.

4a) Of the above claim(s) *9-14* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-4 and 6-8* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☒ Other: *Declaration*.

DETAILED ACTION

Remarks

The amendments and arguments filed 08/26/2009 have been entered and considered. Claims 1-4 and 6-14 are pending. Claims 9-14 are withdrawn. Claims 1-4 and 6-8 are under examination. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Claim Rejections - 35 USC § 102 - withdrawn

The rejection of claims 1-7 under 35 U.S.C. 102(a) as being anticipated by Jeong, et al. (2003) is withdrawn. Applicant's declaration under 37 C.F.R. § 1.132 has obviated the rejection.

Claim Rejections - 35 USC § 102 - New

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1, 3, 4, and 6 are rejected under 35 U.S.C. 102(b) as being anticipated by Cook, et al. (U.S. Patent 5,717,083) as evidenced by Agrawal et al., (Proc. Natl. Acad. Sci, 1988, 85, 7079-7083) and www.newton.dep.anl.gov (of record).

Cook, et al. teaches oligomeric compounds comprising a phosphoroamidate-linked PEG (column 3, line 46 to column 5, line 8). The oligomeric compounds include 20-nucleotide

oligomeric compounds (column 4 where A is a purine or pyrimidine, and *d2*=0, L is a heterocycle, and *m*=20). Cook teaches that the oligomeric compounds of the invention include antisense oligonucleteotides as indicated by Cook's reference in column 3 to Agrawal, et al., who teach antisense oligonucleotides targeting HIV. According to the website, www.newton.dep.anl.gov, a 20-nucleotide single-stranded DNA molecule has a molecular weight of approximately 6600 daltons (330 daltons per nucleotide). Thus, Cook, et al. clearly anticipate the instant claims.

Claim Rejections - 35 USC § 103 - maintained

Claims 1-4, 6, and 7 are rejected under 35 U.S.C. 103(a) as being unpatentable over Tullis (1990, US Patent 4,904,582, of record) and Goodchild (1990, Bioconj. Chem., v.1:165-187, of record). This rejection is maintained for the reasons of record and as clarified herein to address the claim amendments.

Tullis describes oligonucleotide conjugates for transport across cellular membranes for modulating gene expression (abstract). In Table 1 in column 19, Tullis discloses the "MBF 20 antisense C_2-PEG" probe that is antisense to mouse Beta-globin mRNA and comprises a 20-nucleotide phosphodiester-linked molecule conjugated to PEG (M_r = 3500). According to the website, www.newton.dep.anl.gov, a 20-nucleotide single-stranded DNA molecule has a molecular weight of approximately 6600 daltons (330 daltons per nucleotide). Tullis teaches that the PEG group can be added to 5'- or 3'-end of the antisense oligonucleotide by various protocols (column 5 line 44 to column 6 line 8). Tullis does not teach the antisense oligonucleotide covalently linked to PEG via a phosphoroamidate linkage or an acetal bond.

Goodchild teaches that conjugate groups can be covalently linked to oligonucleotides by phosphoroamidate linkage (page 168, third paragraph; page 170, section *ii*, "Incorporation of Non-Nucleotides").

It would have been obvious to make the antisense oligonucleotide-PEG conjugate taught by Tullis with a phosphoroamidate linkage as the covalent linkage between PEG and the ODN. Tullis teaches that various protocols for linking PEG to ODNs can be used and Goodchild teaches that phosphoroamidate linkage is a protocol for doing so. Thus, one of skill in the art would recognize the phosphoroamidate linkage as a simple substitution of one PEG-ODN linkage for another. Therefore, claims 1-7 would have been obvious to one of skill in the art at the time of the instant application.

Response to arguments

Applicant argues that the amendments to the claims have rendered the claims non-obvious over the cited references. This is not persuasive because the Goodchild reference teaches conjugation of conjugate groups via phosphoroamidate linkages as instantly claimed.

Claims 1-4 and 6-8 rejected under 35 U.S.C. 103(a) as being unpatentable over Tullis and Goodchild as applied to claims 1-7 above, and further in view of Bennett, *et al.* (1994, J. Clin. Invest., v.93:820-828, of record). This rejection is maintained for the reasons of record and as clarified herein to address the claim amendments.

Claims 1-7 are described above. Claim 8 is to a conjugate for gene transfer comprising a *c-myb*-targeted antisense oligonucleotide covalently linked to a hydrophilic polymer.

Bennett, *et al.* teach *c-myc*-targeted antisense oligonucleotides and inhibition of *c-myc* expression with the antisense oligonucleotides (abstract; pp.822-5). The oligonucleotides were useful for reducing neointimal formation following balloon injury to rat arteries (p.825) and may serve as useful therapeutics for prevention of angioplasty-induced pathologies (p.828). Bennett, *et al.* do not teach *c-myc* antisense oligonucleotides covalently linked to a hydrophilic polymer via a phosphoroamidate linkage or an acetal bond.

Tullis teaches oligonucleotides conjugated to PEG as described above (35 USC §102 rejection). Tullis teaches that the oligonucleotide-polymer conjugates are "more efficient in membrane transport, so as to be capable of crossing the membrane and effectively modulating a transcriptional system" (Abstract). At column 2, "Description of the Specific Embodiments", Tullis explains that "the amphiphilic nature of the product [oligonucleotide-polymer conjugates] aids in the transport of the conjugate across the cellular membrane and can provide additional advantages, such as increasing aqueous or liquid solubility of nucleic acid derivatives."

Goodchild teaches that conjugate groups such as PEG can be covalently linked to oligonucleotides via a phosphoroamidate linkage (page 168, third paragraph; page 170, section *ii*, "Incorporation of Non-Nucleotides").

It would have been obvious to make a *c-myc*-targeted antisense oligonucleotide as taught by Bennett, *et al.* conjugated to PEG as taught by Tullis and linked via a phosphoroamidate linkage as taught by Goodchild. One would have been motivated to make the antisense conjugate because Bennett, *et al.* demonstrated that targeting *c-myc* by antisense was useful for reducing *c-myc* expression and neointimal formation following balloon injury and that such antisense may serve as a therapeutic for angioplasty-induced pathologies. One would be

motivated to conjugate the antisense oligonucleotide (ODN) to PEG because Tullis taught that conjugating ODNs to polymers such as PEG provided more efficient transmembrane transport of the oligonucleotides. One would have recognized that a phosphoroamidate linkage was one of several means of conjugating PEG to the ODN, as taught by Goodchild and described in the previous rejection. One would have a reasonable expectation of success in making the conjugates because Tullis demonstrated successful use of such conjugates for targeting the mouse Beta-globin mRNA (see 35 USC §103 rejection above) and Goodchild teaches that phosphoroamidate linkage is one of several means by which to add conjugate groups to ODNs (pp171-2). Thus, the instant claims would have been obvious to one skilled in the art at the time of the instant application.

Response to arguments

Applicant argues that the amendments to the claims have rendered the claims non-obvious over the cited references. This is not persuasive because the Goodchild reference teaches conjugation of conjugate groups via phosphoroamidate linkages as instantly claimed.

Conclusion

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to JENNIFER PITRAK whose telephone number is (571)270-3061. The examiner can normally be reached on Monday-Friday, 8:30AM-5:00PM, EST.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Tracy Vivlemore can be reached on 571-272-2914. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Jennifer Pitrak
Examiner
Art Unit 1635

/Richard Schnizer/
Primary Examiner, Art Unit 1635